Surgically treated primary cardiac tumors in early infancy and childhood

Massimo A. Padalino, MD,[a] Cristina Basso, MD, PhD,[b] Ornella Milanesi, MD,[c] Vladimiro L. Vida, MD,[a] Giorgio Svaluto Moreolo, MD,[c] Gaetano Thiene, MD,[b] and Giovanni Stellin, MD[a]


Padalino and Basso

Objective: Primary heart tumors in childhood are rare and mostly benign. Surgical treatment is advocated when symptoms or hemodynamic impairment is present.

Materials and Methods: Between 1986 and 2003, 8 children (3 males and 5 females, age ranging 5 days to 6.7 years, median 78 days) with a clinical diagnosis of cardiac mass were treated with surgery. Diagnosis was made by prenatal echocardiography in 3 patients and by 2-dimensional Doppler echocardiography in 5 patients.

Results: Complete surgical excision of the cardiac mass was feasible in all but 1 patient who underwent orthotopic heart transplantation. Surgical pathology examination revealed myxoma in 2 patients, fibroma in 2 patients, rhabdomyoma in 2 patients (multiple in 1), hamartoma in 1 patient, and teratoma in 1 patient. One patient died of cerebral malignancy 38 months after cardiac transplantation. At a mean follow-up of 69.2 months (range 3-190 months), all the remaining patients are asymptomatic, with good ventricular function on 2-dimensional echocardiography and no signs of residual or recurrent tumor.

Conclusion: Surgical excision of obstructive cardiac tumors in childhood is safely feasible. Heart transplantation may represent the only therapeutic option when the tumor extensively invades the ventricular walls. Although 2-dimensional echocardiography remains a reliable diagnostic tool, a definite diagnosis of tumor histotype requires a thorough histopathologic characterization.

CHD

Primary heart tumors are uncommon in patients of pediatric age,[1] with a reported incidence of 0.2% in children referred for cardiac disease,[2] whereas only 14.2% of all cardiac tumors occur in patients aged less than 16 years.[3] Although cardiac myxoma is by far the most common primary heart tumor in adults,[4,5] rhabdomyoma is the most frequently encountered heart tumor in infancy and childhood.[2,6-11] We report on our experience with surgical treatment of primary cardiac tumors in infancy and childhood.

Material and Methods

Between 1986 and 2003, 8 children were treated with surgery because of an echocardiographic diagnosis of cardiac tumor.

Follow-up data were obtained from clinical visits or collected from their referring physicians.

Demographic, clinical, and diagnostic data are summarized in Table 1. The median age at operation was 78 days, ranging from 5 days to 6.7 years; 6 of 8 patients (75%) were younger than 5 months.

All resected masses were sent for gross examination and histologic characterization. Specimens were fixed in formalin, routinely processed for light microscopy, and stained with hematoxylin-eosin, Alcian periodic-acid Schiff, Azan trichrome, and elastic Weigert van Gieson. Immunohistochemistry with a large panel of monoclonal and polyclonal antibodies was performed in selected cases.

From the Division of Pediatric Cardiovascular Surgery,[a] Institute of Pathology,[b] and Department of Pediatrics,[c] University of Padova Medical School, Padova, Italy.

Received for publication June 4, 2004; revisions received Sept 20, 2004; accepted for publication Oct 11, 2004.

Address for reprints: Cristina Basso, MD, PhD, Institute of Pathology, University of Padova Medical School, Via A. Gabelli, 61 35121 Padova, Italy (E-mail: cristina.basso@unipd.it).

J Thorac Cardiovasc Surg 2005;129:1358-63

0022-5223/$30.00

doi:10.1016/j.jtcvs.2004.10.020

TABLE 1. Clinical and surgical data

Patient no.	Sex	Age	Weight (kg)	Presenting symptoms/ signs	Fetal 2D-echo	ECG	C/T index	Site	Surgery	CPB (min)	ACC (min)	Minimal temperature (°C)	Ventilation (h)	ICU (d)	Hospital (d)	Follow-up (mo)
1	M	6.7 y	25.3	Cerebral stroke	N	SR	0.6	LA	Excision	68	49	25	5	1	11	Alive (190)
2	F	42 d	2.9	CHF	Y	SR	0.56	LV	HTX	100	80	25	144	31	33	Dead (38)
3	M	5 d	3.0	Arrhythmia	Y	PSVT	0.73	RA	Excision + RA plasty	39	15	19	10	1	8	Alive (86)
4	F	127 d	5.7	CHF	N	SR	0.52	RV	Excision + RV plasty	110		19	18	3	12	Alive (80)
5	M	114 d	6.1	Loud systolic murmur	N	SR	0.5	RVOT	Excision	32	-	32	8	1	6	Alive (76)
6	F	12 d	2.6	Pericardial effusion	Y	SR	0.73	Extra-cardiac	Excision	-	-	-	8	1	12	Alive (45)
7	F	2.7 y	9.9	CHF	N	SR	0.6	LA	Excision	60	34	26	19	1	8	Alive (36)
8	F	6 d	3.4	Loud systolic murmur	N	SR	0.53	RV	Excision	63	-	32	6	1	8	Alive (3)

ACC, Aortic crossclamping; *CHF,* congestive heart failure; *CPB,* cardiopulmonary bypass; *C/T,* cardiothoracic; *2D-echo,* 2-dimensional echocardiography; *ECG,* electrocardiogram; *F,* female; *HTX,* heart transplantation; *ICU,* intensive care unit; *LA,* left atrium; *LV,* left ventricle; *M,* male; *PSVT,* paroxysmal supraventricular tachycardia; *RA,* right atrium; *RV,* right ventricle; *RVOT,* right ventricular outflow tract; *SR,* sinus rhythm.

CHD

Results

Clinical presentation was congestive heart failure in patients 2, 4, and 7, multiple cerebral strokes in patient 1, and paroxysmal supraventricular tachycardia in patient 3. The remaining 3 patients were mildly symptomatic, and diagnosis was achieved because of loud systolic murmur in patients 5 and 8 and prenatal 2-dimensional echocardiography as a second level screening at week 33 of gestation in patient 6.

Prenatal 2-dimensional echocardiographic diagnosis of cardiac mass was achieved in 3 patients (patients 2, 3, and 6) and then confirmed postnatally. In the 5 remaining patients, the cardiac mass was discovered postnatally as part of the diagnostic investigation by 2-dimensional echocardiography with Doppler examination.

All patients but 1 (patient 3, who presented with paroxysmal supraventricular tachycardia) were in sinus rhythm at preoperative electrocardiogram.

Chest x-ray film showed cardiomegaly in 5 patients, with a mean cardiothoracic ratio of 0.64 and signs of pulmonary congestion in 3 patients. Additional cardiac imaging techniques were used in patients 2 and 4 (computed tomography scan and magnetic resonance imaging, respectively) to clarify the extension of the mass and myocardial wall involvement. Preoperative surgical myocardial biopsy was performed in patient 4, and intraoperative surgical pathology examination of the cardiac mass was performed in patient 8. Surgical intervention consisted of excision of the cardiac mass in 7 patients, and orthotopic heart transplantation was performed in 1 patient (patient 2). Cardiopulmonary bypass was used in all but patient 6 (Table 1). Main gross and histopathologic features are reported in Table 2.

A sessile myxoma of the left atrium was excised in 2 patients: in patient 1, it was in the posterior wall between the interatrial septum and the right superior pulmonary vein orifice; in patient 7 it was between the mitral valve annulus and the right inferior pulmonary vein orifice. Gross examination revealed a gelatinous, villous neoformation in both patients; histologic examination showed an abundant acid-mucopolysaccharide–rich matrix with polygonal, stellate cells with scant eosinophilic cytoplasm scattered throughout. Tumor cells were mostly single, isolated cells without forming vascular or pseudoglandular structures.

Two patients had ventricular fibroma. Patient 4 underwent extended demolition of the right ventricular (RV) free wall to excise a huge fibroma and required RV free-wall reconstruction with a patch. A surgical biopsy was performed first to clarify diagnosis, and it showed abundant proliferation of fibroblasts with collagen deposition, in keeping with cardiac fibroma. Diagnosis was confirmed subsequently by histologic examination of the resected mass. Surgical resection of the mass was not feasible in patient 2, who presented with a huge fibroma invading the whole left ventricular cavity, mimicking a hypoplastic left heart syndrome. This patient had been kept on prostaglandin E_1 since birth for 38 days, until a suitable heart donor became available. Orthotopic heart transplantation was successfully performed after the

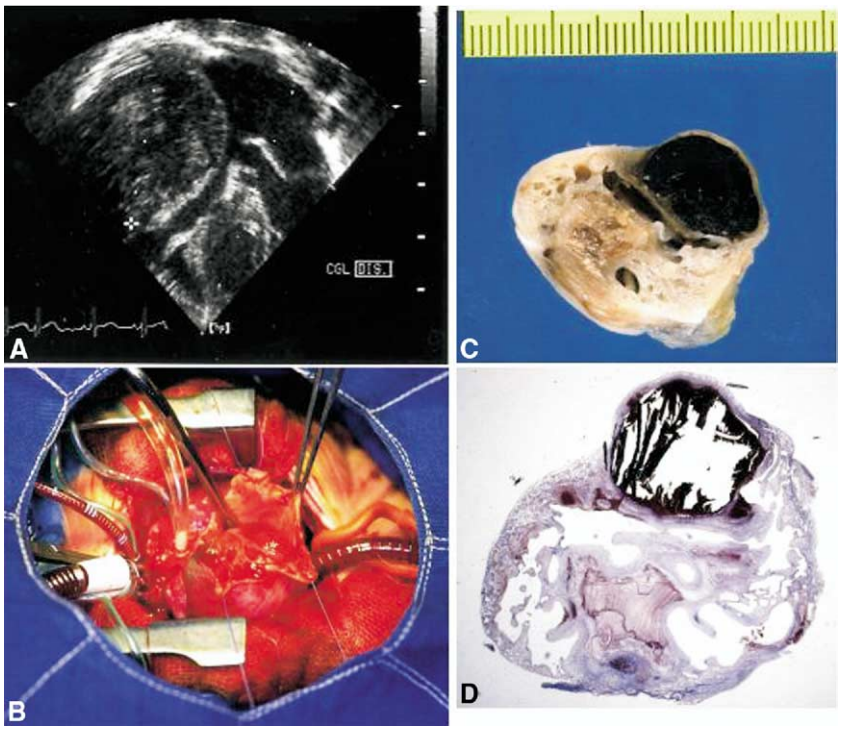

Figure 1. A 5-day-old newborn (patient 3) with paroxysmal supraventricular tachycardia and fetal diagnosis of cardiac mass. A, Postnatal preoperative 2-dimensional echocardiography, subcostal 4-chamber view: Note a round dyshomogeneous mass within the right atrial cavity. B, Surgical view of the mass: Through standard right atriotomy, a sessile reddish mass (32×28×26 mm) was identified, occupying the whole atrial cavity. It was easily detached from the fossa ovalis. C, Cross-section of the resected mass (32×28×26 mm in size) showing the multiple vascular spaces filled with blood. D, Corresponding panoramic histologic view (trichrome Azan ×3).

TABLE 2. Gross and histopathologic findings

Patient no.	Tumor histotype	Location of tumor	Growth	Size (mm)	Weight (g)
1	Myxoma	LA	Endocavitary	40×50×30	25
2	Fibroma	LV free wall	Intramural	50×35×30	70
3	Vascular hamartoma	RA	Endocavitary	32×28×26	11
4	Fibroma	RV free wall	Intramural	60×50×40	81
5	Rhabdomyoma	RVOT	Endocavitary	10×8×8	0.4
6	Teratoma	Extracardiac, ascending aorta	Extracardiac	25×20×15	5.3
7	Myxoma	LA	Endocavitary	35×20×25	9.4
8	Rhabdomyoma	RVOT	Endocavitary	12×10×5	0.4

LA, Left atrium; *LV,* left ventricle; *RA,* right atrium; *RV,* right ventricle; *RVOT,* right ventricular outflow tract.

Shumway technique, with no complications. The donor was a 3-month-old baby weighing 7 kg. Histologic and immunohistochemical examination revealed a non-encapsulated proliferation of fibroblasts embedded within a network of collagen and elastic fibers that dissociated and entrapped few myocytes.

A sessile vascular hamartoma (hemangioma) occupying the whole right atrial cavity was detached from the fossa ovalis in 1 patient (patient 3, Figure 1). The resected mass consisted of dilated vascular channels (cavernous-capillary type) lined by endothelial cells and filled with blood; calcific deposits and areas of hemorrhage were also visible.

A rhabdomyoma, implanted on the RV free wall, impinging the outflow tract and leaning on the pulmonary valve cusps, was gently detached and repaired in 2 patients

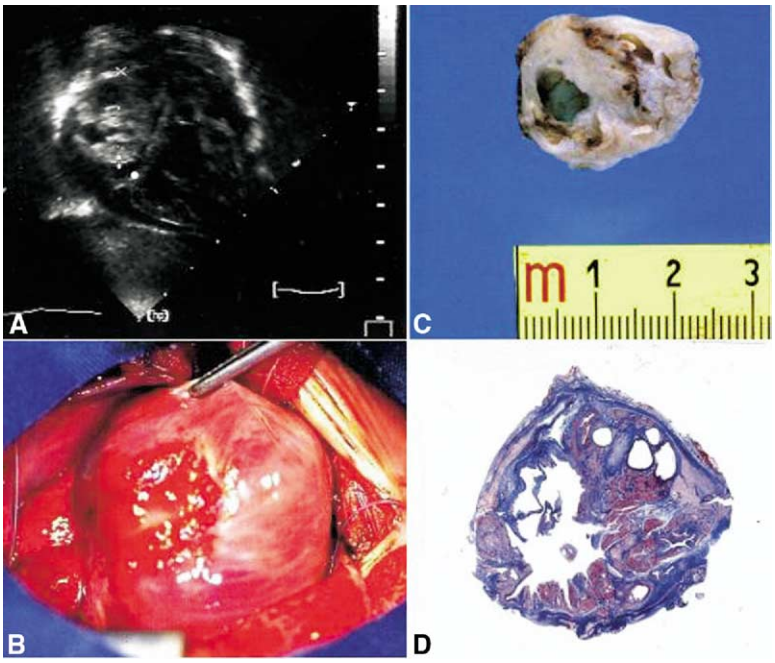

Figure 2. A 12-day-old child (patient 6) with pericardial effusion. A, Postnatal preoperative 2-dimensional echocardiography, subcostal 4-chamber view: Note the cystic dyshomogeneous mass at the base of great vessels. B, Surgical view of the extracardiac mass: After pericardiotomy, a pedunculated extracardiac roundish mass (25×20×15 mm) was isolated. It originated from the ascending aorta, and its arterial supply arose from the aortic vasa vasorum. C, Cross-section of the resected mass (25×20×15 mm) revealing the multicystic appearance. D, Corresponding panoramic histologic view (trichrome Azan ×3).

(patients 5 and 8). At histologic examination, the typical findings of spider cells (showing myofibrils with characteristic cross-striations) were found. Immunohistochemistry results were positive for myoglobin, desmin, and muscle-actin.

In 1 case (patient 6, Figure 2), there was a pedunculated extracardiac teratoma, originating from the ascending aorta, with arterial supply originating from the aortic vasa vasorum. Histology revealed a typical teratoma with multicystic appearance and evidence of endodermal-, ectodermal-, and mesodermal-derived cells.

All patients were discharged in excellent hemodynamic condition and sinus rhythm after a mean stay of 12.2 days. Predischarge 2-dimensional echocardiography showed good left ventricular function (mean left ventricle ejection fraction: 72%) and no residual masses in all patients.

At a mean follow-up of 69.2 months (3-190 months), patient 2 died of cerebral astrocytoma 38 months after heart transplantation, whereas all the remaining patients are alive and in good clinical condition with no cardiac-related therapy. Patients 1 and 5 are receiving oral therapy for epilepsy and tuberous sclerosis, respectively. Electrocardiogram shows that sinus rhythm and Holter monitoring are within normal limits in all patients. Two-dimensional echocardiography detects good ventricular function (ejection fraction: 75%; shortening fraction: 43.5%); no residual valve regurgitation or recurrent cardiac masses are found.

Discussion

Primary cardiac tumors in the pediatric age group are rare.[1-4] Only a few medical centers can rely on a broad experience with primary cardiac tumors in infancy, and limited surgical series have been described.[2,8,9]

Despite the relatively high frequency in our series, cardiac myxoma in infancy is usually rare compared with the adult population.[4,7] Clinical manifestation includes symptoms and signs of tumor embolism, cavity or valve obstruction, and constitutional symptoms.[6,7] Because of the rapid growth of tumor mass in small-sized cavities, congestive heart failure has been frequently reported in childhood and surgical treatment is lifesaving.

Cardiac fibroma is the second most common tumor of childhood in autopsy series after rhabdomyoma, but it ranks first in surgical series.[3,4] The tumors are usually single masses and most often arise in the left ventricular free wall, whereas RV free-wall and atrial involvement are rare.[6,12] The spectrum of clinical presentation is wide, including congestive heart failure, heart murmurs, and

sudden death.[7] Both of our patients presented with congestive heart failure caused by the large size of the tumor. Spontaneous regression of fibromas has never been described,[6] and surgery is usually required. Midterm excellent results after partial resection of fibromas, with 100% freedom from recurrence of tumoral mass, have been reported.[13] Bidirectional cavopulmonary connection has been associated with subtotal resection of RV fibroma to unload the RV.[14] In the setting of huge, unresectable mass, infiltrating cardiac walls transplantation may be the only therapeutic option.[15]

Rhabdomyoma is the most common intracardiac tumor diagnosed in infancy.[2,6-8] The tumors are usually multiple, most often involving the ventricular myocardium but sometimes projecting into the cavity or freely moving as a pedunculated mass.[6] Ventricular inflow or outflow tracts obstruction, arrhythmia, atrioventricular block, pericardial effusion, and even sudden death have been reported as clinical presentation.[7,16] Potential spontaneous regression,[2,4,7,8] which justifies eventual subtotal resection or even a nonsurgical approach, and the close association with tuberous sclerosis[7,8,17] are described. However, the presence of severe ventricular outflow tract obstruction, as in our cases, may require emergency surgical treatment to avoid hemodynamic impairment.[9-11]

Vascular hamartomas (or hemangiomas) are rare benign neoplasms.[18] They have been described at all ages; they may present with arrhythmias, pericardial effusion, congestive heart failure, extracardiac obstruction, and coronary insufficiency.[19] In symptomatic patients, surgery is usually a highly effective and safe therapy.

Intrapericardial teratomas are rare primary cardiac tumors that typically arise within the pericardium from a pedicle at the base of the great vessels.[3,6,7] Although benign, they may vary in size, often enlarging up to 15 cm.[20] Virtually all intrapericardial teratomas are associated with pericardial effusion,[21,22] which can cause signs and symptoms of heart compression.[7] Complete surgical excision of these tumors is usually curative, without the need for cardiopulmonary bypass.[20,22]

In our limited but heterogenous experience with cardiac tumors in infancy, surgical resection of cardiac tumor has proved to be safe and technically feasible, even in early infancy; surgery usually has been definitive, and reoperation has not been required. The only limitation to a conservative surgical approach has been the extensive invasion by the tumor mass of the myocardium, a condition in which transplantation may remain the only therapeutic chance.

Experience with fetal recognition of cardiac tumors has been gained,[6] and the incidence of cardiac tumor at prenatal diagnosis has been estimated to be 0.14%.[23] Prenatal diagnosis of cardiac tumors was feasible in 38% of cases in our series. Thus, primary cardiac tumors are now amenable to effective surgery even in the first days of life, resulting in the early restoration of the normal cardiac physiology and prevention of life-threatening complications.

According to our experience, 2-dimensional echocardiography remains a highly reliable imaging diagnostic tool, and all other diagnostic imaging techniques remain complementary.[16,24] However, precise information on the tumor histotype is not attainable by echocardiography. A correct therapeutic plan requires an accurate histopathologic diagnosis of the resected mass to rule out the rare case of a malignancy. Preoperative or intraoperative surgical pathology diagnosis on frozen sections may be useful in some instances, as in 2 of our cases, to determine the feasibility and extent of surgical resection.

Despite the severity of presenting symptoms of some tumors in the neonatal period, midterm follow-up results are strongly encouraging. Thus, we advocate surgical treatment of symptomatic cardiac tumors in childhood, because although they are mostly benign, they frequently present a "malignant" hemodynamic behavior.

CHD

References

1. Fyler DC. Report of the New England Regional Infant Cardiac Program. *Pediatrics.* 1980;65:376-461.
2. Beghetti M, Gow RM, Haney I, Mawson J, Williams WG, Freedom RM. Pediatric primary benign cardiac tumors: a 15 year review. *Am Heart J.* 1997;134:1107-14.
3. Burke A, Virmani R. Tumors of the heart and great vessels. In: Atlas of Tumor Pathology. Washington, DC: Armed Force Institute of Pathology; series 3, fascicle 16.
4. Basso C, Valente M, Poletti A, Casarotto D, Thiene G. Surgical pathology of primary cardiac and pericardial tumors. *Eur J Cardiothor Surg.* 1997;12:730-8.
5. Bortolotti U, Maraglino G, Rubino M, et al. Surgical excision of intracardiac myxomas: a 20 year follow up. *Ann Thorac Surg.* 1990; 49:449-53.
6. Freedom RM, Lee KJ, MacDonald C, Taylor G. Selected aspects of cardiac tumors in infancy and childhood. *Pediatr Cardiol.* 2000;21: 299-316.
7. Becker AE. Primary heart tumors in the pediatric age group: a review of salient pathologic features relevant for clinicians. *Pediatr Cardiol.* 2000;21:317-23.
8. Chan HSL, Sonley MJ, Moes F, Daneman A, Smith CR, Martin DJ. Primary and secondary tumors of childhood involving the heart, pericardium and great vessels. *Cancer.* 1985;56:825-36.
9. Arciniegas E, Hakimi M, Farooki ZQ, Truccone NJ, Green EW. Primary cardiac tumors in children. *J Thorac Cardiovasc Surg.* 1980; 79:582-91.
10. Corno A, de Simone G, Catena G, Marcelletti C. Cardiac rhabdomyoma: surgical treatment in the neonate. *J Thorac Cardiovasc Surg.* 1984;87:725-31.
11. Jacobs JP, Anastasios KK, Holland FW, Hershowitz K, Ferrer PL, Perryman RA. Surgical treatment for cardiac rhabdomyomas in children. *Ann Thorac Surg.* 1994;58:1552-5.
12. Turi GK, Albala A, Fenoglio JJ. Cardiac fibromatosis: an ultrastructural study. *Hum Pathol.* 1980;11:577-9.
13. Bertolini P, Meisner J, Paek SU, Sebening F. Special considerations on primary cardiac tumours in infancy and childhood. *Thorac Cardiovasc Surg.* 1990;38:164-7.
14. Beghetti M, Haney I, Williams WG, Mawson J, Freedom RM, Gow RM. Massive right ventricular fibroma treated with partial resection and a cavopulmonary shunt. *Ann Thorac Surg.* 1996;62:882-4.

15. Valente M, Cocco P, Thiene G, et al. Cardiac fibroma and heart transplantation. *J Thorac Cardiovasc Surg*. 1993;106:1208-12.
16. Roberts WC. Primary and secondary neoplasms of the heart. *Am J Cardiol.* 1997;80:671-82.
17. Bosi G, Lintermans JP, Pellegrino PA, Svaluto Moreolo G, Vliers A. The natural history of cardiac rhabdomyoma with and without tuberous sclerosis. *Acta Pediatr.* 1996;85:928-31.
18. Enzinger FM, Weiss SW. Benign tumors and tumor-like lesions of blood vessels. In: Enzinger FM, Weiss SW, eds. *Soft tissue tumors.* St. Louis: CV Mosby; 1988:489-532.
19. Burke AP, Johns J, Virmani R. Hemangiomas of the heart: a clinico-pathologic study of 10 cases. *Am J Cardiovasc Pathol.* 1991;13:283-90.
20. Sumner TE, Crowe JE, Klein A, McKone RC, Weaver RL. Intrapericardial teratoma in infancy. *Pediatr Radiol.* 1980;10:51-3.
21. Benatar A, Vaughan J, Nicolini U, Corrin B, Lincoln C. Prenatal pericardiocentesis: its role in the management of intrapericardial teratoma.*Obstet Gynecol.* 1992;79:856-9.
22. Agozzino L, Vosa C, Arciprete P, de Leva F, Cotrufo M. Intrapericardial teratoma in the newborn. *Int J Cardiol.* 1984;5:21-8.
23. Holley DG, Martin GR, Brenner JI, et al. Diagnosis and management of fetal cardiac tumors: a multicenter experience and review of published reports. *J Am Coll Cardiol*. 1995;26:516-20.
24. Fyke FE, Seward JB, Edwards WD, Miller FA, Reeder GS, Schattenberg TT. Primary cardiac tumors: experience with 30 consecutive patients since the introduction of two-dimensional echocardiography. *J Am Coll Cardiol*. 1985;5:1465-73.